

METHOD AND APPARATUS FOR A MULTIPOLE ION TRAP  
ORTHOGONAL TIME-OF-FLIGHT MASS SPECTROMETER

1 TECHNICAL FIELD OF THE INVENTION

2       The present invention relates generally to means and method  
3 whereby ions can be transferred efficiently from an ion source in  
4 such a way that can be readily analyzed in a time-of-flight (TOF)  
5 mass spectrometer. More specifically, an apparatus is described  
6 which uses an ion trap and a multipole ion guide to obtain higher  
7 resolution from an orthogonal TOF mass spectrometer.

8  
9 BACKGROUND OF THE PRESENT INVENTION

10       The apparatus and methods for ionization described herein are  
11 enhancements of the techniques that are referred to in the  
12 literature relating to mass spectrometry. Mass spectrometry is an  
13 important tool in the analysis of a wide range of chemical  
14 compounds. Specifically, mass spectrometers can be used to  
15 determine the molecular weight of sample compounds. The analysis  
16 of samples by mass spectrometry consists of three main steps -  
17 formation of gas phase ions from sample material, mass analysis of  
18 the ions to separate the ions from one another according to ion  
19 mass, and detection of the ions. A variety of means exist in the  
20 field of mass spectrometry to perform each of these three

1 functions. The particular combination of means used in a given  
2 spectrometer determine the characteristics of that spectrometer.

3 To mass analyze ions, for example, one might use a magnetic  
4 (B) or electrostatic (E) analyzer. Ions passing through a magnetic  
5 or electrostatic field will follow a curved path. In a magnetic  
6 field the curvature of the path will be indicative of the momentum-  
7 to-charge ratio of the ion. In an electrostatic field, the  
8 curvature of the path will be indicative of the energy-to-charge  
9 ratio of the ion. If magnetic and electrostatic analyzers are used  
10 consecutively, then both the momentum-to-charge and energy-to-  
11 charge ratios of the ions will be known and the mass of the ion  
12 will thereby be determined. Other mass analyzers are the  
13 quadrupole (Q), the ion cyclotron resonance (ICR), the time-of-  
14 flight (TOF), and the quadrupole ion trap analyzers. The analyzer  
15 which accepts ions from the ion guide described here may be any of  
16 a variety of these.

17 Before mass analysis can begin, however, gas phase ions must  
18 be formed from sample material. If the sample material is  
19 sufficiently volatile, ions may be formed by electron ionization  
20 (EI) or chemical ionization (CI) of the gas phase sample molecules.  
21 For solid samples (e.g. semiconductors, or crystallized  
22 materials), ions can be formed by desorption and ionization of

1 sample molecules by bombardment with high energy particles.  
2 Secondary ion mass spectrometry (SIMS), for example, uses keV ions  
3 to desorb and ionize sample material. In the SIMS process a large  
4 amount of energy is deposited in the analyte molecules. As a  
5 result, fragile molecules will be fragmented. This fragmentation  
6 is undesirable in that information regarding the original  
7 composition of the sample -- e.g., the molecular weight of sample  
8 molecules -- will be lost.

9 For more labile, fragile molecules, other ionization methods  
10 now exist. The plasma desorption (PD) technique was introduced by  
11 Macfarlane et al. in 1974 (Macfarlane, R. D.; Skowronski, R. P.;  
12 Torgerson, D. F., *Biochem. Biophys. Res Commoun.* **60** (1974) 616).  
13 Macfarlane et al. discovered that the impact of high energy (MeV)  
14 ions on a surface, like SIMS would cause desorption and ionization  
15 of small analyte molecules, however, unlike SIMS, the PD process  
16 results also in the desorption of larger, more labile species --  
17 e.g., insulin and other protein molecules.

18 Lasers have been used in a similar manner to induce desorption  
19 of biological or other labile molecules. See, for example,  
20 VanBreeman, R.B.; Snow, M.; Cotter, R.J., *Int. J. Mass Spectrom.*  
21 *Ion Phys.* **49** (1983) 35; Tabet, J.C.; Cotter, R.J., *Anal. Chem.* **56**  
22 (1984) 1662; or Olthoff, J.K.; Lys, I.; Demirev, P.; Cotter, R.

1 J., *Anal. Instrument.* **16** (1987) 93. Cotter et al. modified a CVC  
2 2000 time-of-flight mass spectrometer for infrared laser desorption  
3 of involatile biomolecules, using a Tachisto (Needham, Mass.)  
4 model 215G pulsed carbon dioxide laser. The plasma or laser  
5 desorption and ionization of labile molecules relies on the  
6 deposition of little or no energy in the analyte molecules of  
7 interest. The use of lasers to desorb and ionize labile molecules  
8 intact was enhanced by the introduction of matrix assisted laser  
9 desorption ionization (MALDI) (Tanaka, K.; Waki, H.; Ido, Y.;  
10 Akita, S.; Yoshida, Y.; Yoshida, T., *Rapid Commun. Mass Spectrom.*  
11 **2** (1988) 151 and Karas, M.; Hillenkamp, F., *Anal. Chem.* **60** (1988)  
12 2299). In the MALDI process, an analyte is dissolved in a solid,  
13 organic matrix. Laser light of a wavelength that is absorbed by  
14 the solid matrix but not by the analyte is used to excite the  
15 sample. Thus, the matrix is excited directly by the laser, and the  
16 excited matrix sublimates into the gas phase carrying with it the  
17 analyte molecules. The analyte molecules are then ionized by  
18 proton, electron, or cation transfer from the matrix molecules to  
19 the analyte molecules. This process, MALDI, is typically used in  
20 conjunction with time-of-flight mass spectrometry (TOFMS) and can  
21 be used to measure the molecular weights of proteins in excess of  
22 100,000 daltons.

1        Atmospheric pressure ionization (API) includes a number of  
2 methods. Typically, analyte ions are produced from liquid solution  
3 at atmospheric pressure. One of the more widely used methods,  
4 known as electrospray ionization (ESI), was first suggested by Dole  
5 et al. (M. Dole, L.L. Mack, R.L. Hines, R.C. Mobley, L.D. Ferguson,  
6 M.B. Alice, *J. Chem. Phys.* **49**, 2240, 1968). In the electrospray  
7 technique, analyte is dissolved in a liquid solution and sprayed  
8 from a needle. The spray is induced by the application of a  
9 potential difference between the needle and a counter electrode.  
10 The spray results in the formation of fine, charged droplets of  
11 solution containing analyte molecules. In the gas phase, the  
12 solvent evaporates leaving behind charged, gas phase, analyte ions.  
13 Very large ions can be formed in this way. Ions as large as 1 MDa  
14 have been detected by ESI in conjunction with mass spectrometry  
15 (ESMS).

16        Many other ion production methods might be used at atmospheric  
17 or elevated pressure. For example, MALDI has recently been adapted  
18 by Victor Laiko and Alma Burlingame to work at atmospheric pressure  
19 (Atmospheric Pressure Matrix Assisted Laser Desorption Ionization,  
20 poster #1121, 4<sup>th</sup> International Symposium on Mass Spectrometry in  
21 the Health and Life Sciences, San Francisco, Aug. 25 - 29, 1998)  
22 and by Standing et al. at elevated pressures (Time of Flight Mass

1 Spectrometry of Biomolecules with Orthogonal Injection +  
2 Collisional Cooling, poster #1272, 4<sup>th</sup> International Symposium on  
3 Mass Spectrometry in the Health and Life Sciences, San Francisco,  
4 Aug. 25 - 29, 1998; and Orthogonal Injection TOFMS *Anal. Chem.*  
5 71(13), 452A (1999)). The benefit of adapting ion sources in this  
6 manner is that the ion optics and mass spectral results are largely  
7 independent of the ion production method used.

8 An elevated pressure ion source always has an ion production  
9 region (wherein ions are produced) and an ion transfer region  
10 (wherein ions are transferred through differential pumping stages  
11 and into the mass analyzer). The ion production region is at an  
12 elevated pressure -- most often atmospheric pressure -- with  
13 respect to the analyzer. The ion production region will often  
14 include an ionization "chamber" (e.g. FIG. 1, ionization chamber  
15 4). In an ESI source, for example, liquid samples are "sprayed"  
16 into the "chamber" to form ions.

17 Once the ions are produced, they must be transported to the  
18 vacuum for mass analysis. Generally, mass spectrometers (MS)  
19 operate in a vacuum between  $10^{-4}$  and  $10^{-10}$  torr depending on the  
20 type of mass analyzer used. In order for the gas phase ions to  
21 enter the mass analyzer, they must be separated from the background  
22 gas carrying the ions and transported through the single or

1 multiple vacuum stages.

2 The use of multipole ion guides has been shown to be an  
3 effective means of transporting ions through vacuum regions.  
4 Publications by Olivers et. al. (Anal. Chem, Vol. 59, p. 1230-1232,  
5 1987), Smith et. al. (Anal. Chem. Vol. 60, p. 436-441, 1988) and  
6 U.S. Pat. No. 4,963,736 (1990) have reported the use of an AC only  
7 quadrupole ion guide to transport ions from an API source to a mass  
8 analyzer. A quadrupole ion guide operated in RF only mode,  
9 configured to transport ions is described by Douglas et. al in U.S.  
10 Patent 4,963,736. Multipole ion guides configured as collision  
11 cells are operated in RF only mode with a variable DC offset  
12 potential applied to all rods. Thomson et. al. in U.S. Patent  
13 Number 5,847,386 describes a multipole ion guide assembly  
14 configured to create a DC electric field along the ion guide axis  
15 to move ions axially through a collision cell or to promote  
16 Collision Induced Dissociation (CID) fragmentation.

17 Other schemes are available, which utilize both RF and DC  
18 potentials in order to facilitate the transmission of ions of a  
19 certain range of m/z values. For example, Morris et al., in H.R.  
20 Morris et al., High Sensitivity Collisionally-Activated  
21 Decomposition Tandem Mass Spectrometry on a Novel Quadrupole/  
22 Orthogonal- acceleration Time-of-Flight Mass Spectrometer, Rapid

1 Commun. Mass Spectrom. 10, 889 (1996), uses a series of multipoles  
2 in their design, one of which is a quadrupole. The quadrupole can  
3 be run in a "wide bandpass" mode or a "narrow bandpass" mode. In  
4 the wide bandpass mode, an RF-only potential is applied to the  
5 quadrupole and ions of a relatively broad range of  $m/z$  values are  
6 transmitted. In narrow bandpass mode both RF and DC potentials are  
7 applied to the quadrupole such that ions of only a narrow range of  
8  $m/z$  values are selected for transmission through the quadrupole.  
9 In subsequent multipoles the selected ions may be activated towards  
10 dissociation. In this way the instrument of Morris et al. is able  
11 to perform MS/MS with the first mass analysis and subsequent  
12 fragmentation occurring in what would otherwise be simply a set of  
13 multipole ion guides.

14 Time-of-flight mass spectrometry (or TOFMS) plays an important  
15 role in the analysis of chemical compounds. Specifically, TOF mass  
16 spectrometers are useful in determining the molecular weight of  
17 sample compounds. In orthogonal TOF mass spectrometers ions pass  
18 from the source into the analyzer in a direction which is  
19 orthogonal to the axis of the analyzer. The concept of orthogonal  
20 acceleration using TOFMS was disclosed by O'Halloran et al. in 1964  
21 (G.J. O'Halloran et al., *Determination of Chemical Species*  
22 *Prevalent in a Plasma Jet*. Technical Documentary Report No. ASD-



1 TDR-62-664, prepared under contract AF 33(616)-8374 by the Bendix  
2 Corp. Research Laboratories (1964)). O'Hallran et al. also  
3 introduced the application of TOF mass analysis to ionization  
4 sources at elevated pressure. One advantage to using orthogonal  
5 acceleration and elevated pressure ionization sources is that ions  
6 form a continuous beam and can be mass analyzed more efficiently.  
7 Also, with the "orthogonal acceleration" method, the mass analysis  
8 occurs along an axis which is orthogonal to the ion's initial  
9 direction of motion. As a result, the initial energy of the ions  
10 does not significantly degrade the mass resolution of the  
11 instrument.

12 Chien and Lubman demonstrated the advantage of using a  
13 quadrupole ion trap - TOF mass analyzer in the analysis of  
14 electrospray produced ions (Chien, B.M.; Lubman, D.M., *Anal. Chem.*  
15 *66*, 1630 (1994)). The ions from the electrospray source are  
16 transferred with a high efficiency to the TOF analyzer and ions may  
17 be preselected and collision induced dissociation on these ions may  
18 be performed. One disadvantage with this method is low mass  
19 resolving power. Also, there are restrictions in the time required  
20 for cooling the ions and cycling the pressure in the ion trap.

21 Chernushevich et al discloses the use of ion introduction into  
22 an RF-quadrupole ion guide at a high gas pressure (I.V.

1 Chernushevich, Proceedings of the 44th ASMS Conference of Mass  
2 Spectrometry and Allied Topics, May 12-16, 1173 (1996)).  
3 Similarly, Douglas discloses ion introduction into a quadrupole ion  
4 trap rather than a TOF analyzer (D.J. Douglas, USPN 5,179,278).  
5 Here, the ions are cooled by passage through the quadrupole ion  
6 trap at elevated pressure and are transferred into a low pressure  
7 region containing the TOF analyzer. This "collisional focusing"  
8 method can be incorporated with the "orthogonal acceleration"  
9 method to obtain a higher resolution mass spectra.

10 Morris et al. discloses the use of additional multipole  
11 devices to preselect ions and induce collision dissociation in the  
12 trap - TOF analyzer (H.R. Morris et al., *Rapid Comm. Mass Spectrom.*  
13 **10**, 889 (1996)). Collision induced dissociation experiments were  
14 disclosed in Lubman (B.M. Chien, S.M. Michael, D.M. Lubman, *Int J.*  
15 *Mass Spectrom. Ion Process.*, **131**, 149 (1994), B.M. Chien, D.M.  
16 Lubman, *Anal. Chem.* **66**, 1630 (1994)). There first multipole device  
17 is used to cool ions then a second multipole is used for mass  
18 selection, and a third multipole is used for collision induced  
19 dissociation.

20 In orthogonal TOF mass spectrometer of the invention, ions are  
21 trapped in a multipole ion guide having an apertured electrode at  
22 its exit. By applying a repelling potential to the electrode, ions

1 near the exit of the multipole are reflected back into the guide  
2 for trapping. During analysis, the potential of the electrode is  
3 pulsed so that, during the duration of the pulse (20-100 us), ions  
4 may exit the multipole.

5 Also, ions extracted from a multipole device and orthogonally  
6 accelerated to the direction of the axis of the analyzer will have  
7 a significant kinetic energy orthogonal to the axis of the  
8 analyzer. This initial kinetic energy will cause the ions to drift  
9 perpendicularly to the analyzer axis. This kinetic energy must be  
10 accounted for in order to prevent ion loss and to ensure ion  
11 detection. Also, during the extracting process, accelerated ions  
12 will have its kinetic energy component increased in the direction  
13 axial to the multipole. As the ions enter the accelerator of the  
14 analyzer, the axial energy component will result in a decreased  
15 mass resolution.

16 High efficiency in transmitting ions from the multipole to the  
17 analyzer will require the spatial extent of the ion beam  
18 perpendicular to the axis of the analyzer to be large compared to  
19 that of prior art designs. As a result, some prior art devices  
20 (i.e. the two stage reflectron taught by R. Frye in USPN 4,731,532)  
21 cannot be used with the orthogonal multipole TOF device described  
22 above.

1           An alternative "method and device for orthogonal ion injection  
2 into a time-of-flight mass spectrometer" was proposed in Franzen  
3 United States Pat. No. 5,763,878 (the "'878 patent"). According to  
4 the '878 patent, ions are ejected from a multipole ion guide of  
5 design similar to that of Chernushevich et al. into a time-of-  
6 flight analyzer and in a direction orthogonal to the axis of the  
7 multipole device. In trapping mode an RF potential is applied to  
8 the poles of the multipole device whereas in ejection mode, DC  
9 potentials are applied to the poles of the multipole device so as  
10 to accelerate the ions in a direction orthogonal to the axis of the  
11 multipole device and parallel to the axis of the TOF analyzer.

12           As shown in FIGs. 1 & 2, the '878 patent discloses multipole  
13 devices having six poles (FIG. 1, elements 122-127) or four poles  
14 (FIG. 2, elements 132-135) to trap and eject ions. Although the  
15 spectrometer according to the '878 patent has certain advantages  
16 over prior art, it is not ideal. One disadvantage of the  
17 spectrometer according to the '878 patent is that the multipole  
18 device of the '878 patent has a limited mass-to-charge (" $m/z$ ")  
19 range. The  $m/z$  range of the device can be improved by increasing  
20 the number of poles used -- for example, eight or more could be  
21 used instead of the four or six poles used by the '878 patent.  
22 Using more poles distributed in roughly a circular pattern around

1 the axis of the multipole would improve the  $m/z$  range of the device  
2 while in trapping mode. However, when ejecting ions from the  
3 device, the DC potential applied to each pole would have to be  
4 controlled independently. Thus, in ejection mode, having a large  
5 number of poles would be impractical.

6 Also, according to the '878 patent, the arrangement of  
7 electrodes in the multipole is not ideal for the acceleration of  
8 ions into a TOF analyzer. That is, it is difficult to produce a  
9 uniform electrostatic field which accelerates ions in a direction  
10 orthogonal to the hexapole. The electric field strength and  
11 direction of acceleration of the ions during extraction from  
12 multipole device of the '878 patent is dependent on the ion's  
13 position within the multipole device. The electrostatic field  
14 produced in an ideal TOF ion accelerator is completely homogeneous.  
15 In other words, the electrostatic field strength and the direction  
16 in which the ions are accelerated is not a function of position  
17 within the accelerator.

18 FIG. 1 shows a section through a prior art Ion Trap in the  
19 form of a hexapole with Pole Rods (122) to (127). The hexapole  
20 arrangement is located between the Ion Repeller (121) and the Ion  
21 Drawing Diaphragm (129), spaced about 12 millimeters from one  
22 another. The hexapole arrangement houses the Ion Cloud (128)

1 formed as a thin thread which is made up of well-cooled ions. In  
2 storage conditions, one phase of the storage RF voltage is applied  
3 to Pole Rods (122), (124), and (126), and the other phase to Pole  
4 Rods (123), (125), and (127). Ions of both polarities can be  
5 stored. To outside positive ions, a more positive voltage is  
6 applied to Pole Rods (122) and (125), a more negative voltage to  
7 Rods (124) and (127) than to Rods (123) and (126). The Ion Drawing  
8 Diaphragm (129) is designed as a slit diaphragm through which all  
9 ions can be accelerated without loss. Slight beam divergences can  
10 be focused through the cylindrical Einzel Lens (130) into a  
11 parallel beam. Arrow (131) indicates the flight direction within  
12 the time-of-flight spectrometer.

13 FIG. 2 shows a quadrupole arrangement made up of Pole Rods  
14 (132) to (135). The pole rods are arranged asymmetrically here in  
15 order to cause outpulsing solely through the external electrical  
16 field between the Ion Repeller (121) and Ion Drawing Diaphragm  
17 (129), without special voltages on the Pole Rods (132) to (135),  
18 the RF voltage of which is simply switched off.

19 Also, the multipole device according to Franzen stores ions in  
20 only one dimension. In particular, the '878 patent states that  
21 "ions must be stored in the form of a thin thread in the axis" of  
22 the multipole device. This substantially limits the number of ions

1 which can be stored in the device without encountering space charge  
2 effects.

3  
4 SUMMARY OF THE INVENTION

5 An object of the present invention is to provide an improved  
6 method and apparatus for a multipole ion guide and trap (i.e.,  
7 quadrupole, hexapole, octapole, etc.) for use in orthogonal TOFMS.  
8 Specifically, the multipole ion trap-orthogonal time of flight mass  
9 spectrometer of the present invention comprises an ion source, an  
10 ion guide and trap, two reflectrons, and a detector. The ion guide  
11 is connected downstream of the ion source and is disposed  
12 orthogonal to the ion accelerator. The first reflectron is a two  
13 stage gridless reflectron and it is disposed opposite the  
14 accelerator. The second reflectron is a single stage gridded  
15 reflectron and it is disposed opposite the first reflectron, in  
16 between the ion flight region and the detector.

17 In the present invention, part of the accelerator is a single  
18 trapping device which incorporates RF ion trapping and  
19 electrostatic ion extraction. The device comprises two types of  
20 electrodes--RF/DC electrodes, and DC electrodes. The RF/DC  
21 electrodes are preferably positioned parallel to one another, while  
22 the DC electrodes encompass the RF/DC electrodes. In a preferred

1 embodiment, there are two sets of electrodes, each containing both  
2 the RF/DC electrodes and the DC electrodes. The sets of electrodes  
3 are arranged parallel and adjacent to one another. Also, within  
4 each set of electrodes, the RF/DC and DC electrodes are positioned  
5 in the same plane.

6 During normal operation of the multipole ion trap, the DC  
7 electrodes are held at a fixed DC potential. While trapping ions,  
8 the DC potential (i.e., the time averaged potential) on the RF/DC  
9 electrodes is held at a potential which is more attractive to the  
10 ions than the potential on the DC electrodes. Also, a preferred  
11 geometry of the device is such that the electrostatic field  
12 gradient produced by the electrodes is strong near the DC  
13 electrodes and virtually non-existent near the center. Also, the  
14 RF potentials applied to adjacent RF/DC electrodes are 180 degrees  
15 out of phase to repel ions toward the center of the multipole ion  
16 trap. During trapping, the potential applied to the DC electrodes  
17 must be of sufficient magnitude and the proper polarity to force  
18 ions toward the center of the trap. Preferably, the dimensions of  
19 the trap are chosen so that low energy ions (i.e.,  $< 0.1$  eV) can be  
20 forced toward the center of the trap (i.e., to a region of 5mm  
21 diameter) when trapping and the electrostatic field can be largely  
22 homogeneous during extraction.



1       To extract the ions from the multipole ion trap, the  
2 potentials on the RF/DC electrodes of each plane are held at two  
3 different fixed potentials. The potential difference between the  
4 planes accelerates the ions in a direction normal to the planes.  
5 The geometry, magnitude and the frequency of the potentials are  
6 crucial to the operation of the trap. The diameter of the planes  
7 and the gap between them should provide a small distribution of  
8 starting positions for the TOF analysis so that the potentials  
9 applied to the electrodes for extraction of the ions result in a  
10 short turn around time.

11       An object of the invention is to provide a multipole ion trap  
12 which, during extraction produces an ion beam having a width small  
13 enough (i.e., 5mm in diameter) to be used with any conventional  
14 TOFMS devices. For example, the trap may be used with an RF/DC ion  
15 guide, and the planes of the electrodes of the ion guide are  
16 aligned parallel to the trap's electrodes and the center of the  
17 trap is aligned with the center of the guide. This arrangement  
18 allows the ions to move freely between the ion guide and the trap  
19 when the potential on the connecting (or gate) electrode is  
20 sufficiently low. This gate electrode can be closed by raising its  
21 potential to match that of the other DC electrodes. By slowly  
22 raising the gate potential, nearby ions will be forced into the

1 trap without maintaining a significant amount of kinetic energy.  
2 The potential on the gate electrode is then maintained at the  
3 potential of the DC electrodes during the trapping and extracting  
4 process.

5 In accordance with the invention, the trap is preferably  
6 disposed between and parallel to two planar electrodes and  
7 comprises a fine conducting mesh. The accelerator portion  
8 comprises guard ring electrodes and a gridded electrode which are  
9 aligned parallel to one another and spaced at regular intervals.  
10 While trapping, the electrodes adjacent to the trap are held at  
11 neutral potentials. At this potential, there should be no  
12 significant influence of these electrodes on the ions in the trap.

13 Conversely, during the extraction process, the planar  
14 electrode between the guide and the trap is pulsed to a repulsive  
15 potential, while the electrode between the trap and the accelerator  
16 is pulsed to an attractive potential. This generates a homogenous  
17 electric field with the same field gradient as that of the trap.  
18 The ions then pass through the electrode nearest the guide and can  
19 be accelerated by the electric field generated by the guard rings  
20 and gridded electrodes. In the accelerator portion, the electrodes  
21 are electrically connected by an RC network.

22 An object of the multipole ion trap according to the present

1 invention is to provide simplified and more efficient transfer ion  
2 optics than conventional ion traps and ion guides, as well as prior  
3 art orthogonal TOF mass spectrometers. Another object of the  
4 invention is to provide a multipole ion trap having no significant  
5 dependance on the  $m/z$  range of the instrument on the timing between  
6 the gate and accelerator pulses as in prior art instruments. Yet  
7 another object of the invention is to provide a multipole ion trap  
8 in which there is no dependence of transmission efficiency through  
9 the analyzer on the potential on a deflector often used in  
10 conventional instruments. Yet a further object of the invention is  
11 to provide a multipole ion trap wherein, in a given ion extraction,  
12 more ions can be extracted and analyzed than by conventional means  
13 and methods. In particular, in accordance with the present  
14 invention, all (or substantially all) of the ions within the trap  
15 will be extracted in a single pulse.

16 Other advantages of the present invention over prior art  
17 include improved resolution in the TOF analyzer and the elimination  
18 of correction for the initial orthogonal kinetic energy. These  
19 advantages are the results of using truly thermal kinetic energy  
20 ions. The ions in the trap will have only thermal kinetic energies  
21 because the ions are not accelerated between the ion guide and  
22 trap.

1 Other objects, features, and characteristics of the present  
2 invention, as well as the methods of operation and functions of the  
3 related elements of the structure, and the combination of parts and  
4 economies of manufacture, will become more apparent upon  
5 consideration of the following detailed description with reference  
6 to the accompanying drawings, all of which form a part of this  
7 specification.

8  
9 BRIEF DESCRIPTION OF THE DRAWINGS

10 A further understanding of the present invention can be  
11 obtained by reference to a preferred embodiment set forth in the  
12 illustrations of the accompanying drawings. Although the  
13 illustrated embodiment is merely exemplary of systems for carrying  
14 out the present invention, both the organization and method of  
15 operation of the invention, in general, together with further  
16 objectives and advantages thereof, may be more easily understood by  
17 reference to the drawings and the following description. The  
18 drawings are not intended to limit the scope of this invention,  
19 which is set forth with particularity in the claims as appended or  
20 as subsequently amended, but merely to clarify and exemplify the  
21 invention.

22 For a more complete understanding of the present invention,

1 reference is now made to the following drawings in which:

2 FIG. 1 depicts a prior art hexapole ion trap according to  
3 Franzen United States Patent Number 5,763,878;

4 FIG. 2 depicts a prior art quadrupole ion trap according to  
5 Franzen United States Patent 5,763,878;

6 FIG. 3 is an overall schematic drawing of a time-of-flight  
7 mass analyzer incorporating the present invention;

8 FIG. 4 shows the preferred embodiment of the multipole ion  
9 trap as used with an ion accelerator for use in TOF mass  
10 spectrometry, according to the invention;

11 FIG. 5A shows a side view of the preferred embodiment of a  
12 multipole ion trap according to the present invention;

13 FIG. 5B shows a cross-sectional view of the multipole ion trap  
14 shown in FIG. 5A;

15 FIG. 6 depicts the multipole ion trap shown in FIGs. 4, 5A and  
16 5B as used with an RF/DC ion guide;

17 FIG. 7 shows the multipole ion trap depicted in FIGs. 4, 5A  
18 and 5B as used for an electron capture dissociation (ECD);

19 FIG. 8 demonstrates the introduction of low energy electrons  
20 into the accelerator shown in FIG. 6 to produce negative ions from  
21 neutral gas phase molecules, in accordance with the invention;

22 FIG. 9 is a graph of signal intensity vs. pulse duration

1 showing the intensity of the ion beam as a function of time during  
2 an extraction pulse of 20 microseconds using the accelerator and  
3 multipole ion trap depicted in FIGs. 5A, 5B and 6.  
4

#### 5 DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

6 As required, a detailed illustrative embodiment of the  
7 present invention is disclosed herein. However, techniques,  
8 systems and operating structures in accordance with the present  
9 invention may be embodied in a wide variety of forms and modes,  
10 some of which may be quite different from those in the disclosed  
11 embodiment. Consequently, the specific structural and  
12 functional details disclosed herein are merely representative,  
13 yet in that regard, they are deemed to afford the best embodiment  
14 for purposes of disclosure and to provide a basis for the claims  
15 herein which define the scope of the present invention. The  
16 following presents a detailed description of a preferred  
17 embodiment (as well as some alternative embodiments) of the  
18 present invention.

19 Referring first to FIG. 3, depicted is a schematic drawing  
20 of the preferred embodiment of a multipole ion trap orthogonal  
21 time-of-flight (TOF) mass spectrometer according to the  
22 invention. As shown, the (TOF) mass spectrometer 16 in

1 accordance with the present invention includes ion production  
2 region 1, ion guide 2, accelerator/trap assembly 3, first flight  
3 tube/region 4, first ion reflector 5, second flight tube/region  
4 7, second ion reflector 6, detector 15. Generally, ions are  
5 first generated in ion production region 1, which may be any  
6 known ionization means or method (i.e., electrospray ionization  
7 (ESI), plasma desorption ionization (PD), matrix assisted  
8 laser/desorption ionization (MALDI), electron ionization (EI),  
9 chemical ionization (CI), etc.). At some predetermined time  
10 after formation, the ions are accelerated into ion guide 2 which  
11 transports the ions to accelerator/trap 3. Ion guide 2 is  
12 preferably an RF/DC ion guide. For example, the RF/DC ion guide  
13 comprises a plurality of elongated electrode rods positioned  
14 around a central axis such that when RF & DC potentials are  
15 applied to the electrode rods, an electrostatic field is  
16 generated, thereby allowing the transmission of the ions through  
17 ion guide 2 - from its entrance end (at ion production region 1)  
18 to ion accelerator/trap 3.

19 As the ions exit ion guide 2, they are introduced into  
20 accelerator/trap 3, which, as shown in FIG. 6, preferably  
21 comprises ion trap 10 (as further depicted in FIGs. 5A & 5B)  
22 disposed between and parallel to planar electrodes 17 & 18, a

1 plurality of regularly spaced parallel guard ring electrodes 8  
2 and gridded electrode 19 (which is aligned parallel to guard ring  
3 electrodes 8). Preferably, planar electrodes 17 & 18 are mesh  
4 gridded electrodes, but other forms of apertured electrodes may  
5 be used. The ions first reach ion trap 10 where, in a preferred  
6 embodiment, the ions are trapped for some predetermined time  
7 prior to orthogonal acceleration into the mass analyzer.

8 Preferably, ion trap 10, as shown in FIGs. 5A and 5B, comprises  
9 two substantially parallel planar series of electrodes (i.e.,  
10 each series of electrodes comprises, preferably, six RF/DC  
11 electrode rods 12 aligned in parallel and in a single plane, and  
12 two curved DC cap electrodes 13, as depicted in FIGs. 5A & 5B).  
13 Preferably, RF/DC electrode rods 12 are of lengths such that  
14 there parallel and planar alignment results substantially in a  
15 circular pattern. This allows curved DC cap electrodes 13 to  
16 substantially surround the ends of RF/DC electrodes 12 -- one DC  
17 cap electrode 13 at either end of RF/DC electrode rods 12. Of  
18 course, in accordance with the invention, ion trap 10 may  
19 comprise more or less than six RF/DC electrode rods 12.

20 Depending upon the potential(s) applied to the electrodes of  
21 accelerator/trap 6 (see FIG. 4), the ions are either trapped  
22 therein or accelerated into flight tube/region 8 toward first



1 reflector 10. As shown, accelerator/trap 6/7 is positioned such  
2 that ions may be transferred from ion trap 6 to TOF accelerator 7  
3 which comprises guard ring electrodes 16 and gridded electrodes  
4 36 and 38.

5 Referring now to multipole ion guide 22, as depicted in FIG.  
6 6, a preferred embodiment of multipole ion guide 6 comprises of  
7 RF guide electrodes 40 and is connected to ion trap 20 by a gate  
8 electrode 44. As shown, the ion guide 22 is positioned such that  
9 ions coming from the entrance 42 may be transferred through the  
10 guide 22 and into trap 20 via the gate electrode 44. Diagram 46  
11 in FIG. 6 shows how the potential on the gate electrode can be  
12 varied at the different stages of operation.

13 Turning now to ion trap 20, as depicted in FIGs. 5A and 5B,  
14 a preferred embodiment of ion trap 20 is shown comprising two  
15 sets of electrodes, RF/DC electrodes 24 and DC electrodes 26.  
16 Each set consists of RF/DC electrodes 24 arranged parallel to one  
17 another and DC electrodes 26 which encompass the RF/DC electrodes  
18 24. The electrodes 24 & 26 of each set are arranged in parallel  
19 and adjacent planes. The device depicted in FIGs. 5A and 5B is  
20 only part of the larger accelerator/trap 6 instrument depicted in  
21 FIG. 3. As shown, the ions 28 are trapped in an elongated region  
22 at the center of the trap 20. Also, diagram 52 shows how the

1 voltage will vary at each stage of operation of trap 20. At one  
2 stage of operation the ions 28 will exit the trap and enter the  
3 TOF accelerator as shown in FIG. 3.

4 Next, FIG. 9 shows results of a prior art experiment  
5 involving ions ejected from a multipole ion guide having a pulsed  
6 exit aperture. The ions were trapped in a multipole ion guide by  
7 applying a repelling potential on the apertured electrode at its  
8 exit. A pulse of ions is produced for analysis by pulsing the  
9 aperture electrode. Ions may exit the multipole (in this case a  
10 hexapole) and enter the detector for the duration of the pulse.  
11 FIG. 8 depicts the intensity of the ion beam as a function of  
12 time during an extraction pulse of 20 us. Only a certain fraction  
13 of the ions extracted from the multipole will be between the  
14 repeller and grid simultaneously and only that fraction will be  
15 useful in the TOF analysis. The extraction duration is selected  
16 to optimize this fraction of useful ions.

17 During operation, ions 28 are generated by the ion  
18 production region 2 and are introduced to the accelerator/trap 6  
19 via multipole ion guide 4. The region near the ion entrance 42 is  
20 filled with neutral gas held at moderate pressure to cool the  
21 ions to thermal energies. The pressure of the gas near the trap  
22 20 is relatively low compared to the pressure near the entrance

1 region. The potential on the gate electrode 44 is held at a  
2 potential near ground and ions 28 can pass from the guide to the  
3 trap. As shown in FIG. 6, the gate 44 potential can be closed by  
4 slowly raising its potential until it is the same potential as  
5 the other DC electrodes 26. The ions 28 will not be able to enter  
6 the trap 20, and the trap/extract process may begin. If the  
7 potential energy is raised slowly enough, then the ions 28 forced  
8 into the trap 20 will not have significant kinetic energy.

9 After the ions 28 have passed the multipole guide 22 and  
10 entered the trap 20, the trap 20 is turned on and the ions 28 are  
11 forced into an elongated region near its center. As depicted in  
12 FIGs. 5A and 5B, the electrodes 24 & 26 and their placement in  
13 the trap 20 is out of proportion and is intended only to  
14 illustrate the concept of trapping and extracting ions 28  
15 according to the present invention. In a more practical example,  
16 the RF/DC electrodes 24 might have a diameter of 50 um and the  
17 gap between the planes might be 1 mm. The electrodes 24 need not  
18 be cylindrical but could be, for example, rectangular in cross  
19 section. The planes of RF/DC electrodes 24 might have a diameter  
20 of 10 mm. The DC electrodes 26 might have an inner diameter of  
21 10.1 mm and be biased to a potential of 20 V to trap positive  
22 ions. During trapping mode operation, the RF potential applied to

1 the RF/DC electrodes 24 might take the form of a square wave of a  
2 frequency of 5 MHz, a peak-to-peak voltage of 200 V, and a time  
3 averaged potential of 0V. Adjacent RF/DC electrodes 24 within a  
4 given plane would experience potentials 180 degrees out of phase.  
5 During extraction mode operation, the RF/DC electrodes 24 of one  
6 plane would all be held at a DC potential of 100V whereas the  
7 potential applied to the opposite plane would be -100 V. The  
8 potential difference between the planes of electrodes 24 & 26  
9 accelerates the ions 28 out of the trap 20 in a directions normal  
10 to the planes.

11 As shown in FIG. 4, the extracted ions 28 are transferred  
12 into the TOF ion accelerator 16, 18 & 38. During ion trapping,  
13 the electrodes 34 & 36 are held at neutral potentials. During  
14 extraction, the potential on electrode 34 is pulsed to a  
15 repulsive potential V1. The potential on electrode 36 is pulsed  
16 to an attractive potential V2. V1 and V2 are selected so as to  
17 produce a homogeneous field between electrodes 34 & 36. The  
18 pulsed voltage V2 and the DC potential -HV applied to either end  
19 (36 & 38, respectively) of the RC network 18 is divided and  
20 applied to the electrodes.

21 As depicted in FIG. 3, the ions 28 are accelerated by the  
22 TOF accelerator 7 toward reflectron 10. It is possible to use a

1 two stage reflectron because of the relatively small diameter  
2 (5mm) of the ion beam 8 and 14. In such case, the ions will  
3 then be reflected towards the second reflectron 12 and eventually  
4 end up in the detector 30. However, alternatively the MIT-OTOF  
5 may take the form of a linear reflectron instrument (i.e.,  
6 without the second reflectron, or with two coaxial reflectrons.

7 Next, FIG. 7 shows an alternate embodiment of multiple ion  
8 trap 20 according to the present invention depicting the use of  
9 ion trap 20 with electron capture dissociation ("ECD"). ECD is a  
10 method of forming fragment ions from multiply and positively  
11 charged ions. Specifically, the ions capture low energy  
12 electrons 54. The formed fragments can be analyzed to reveal  
13 structurally useful information about the original ion. A  
14 detailed discussion of the ECD method is given by R.A. Zubarev,  
15 J. Amer. Chem. Soc., 120, 3265 (1998) et al. As shown in FIG. 7,  
16 electrons 54 are injected in a direction parallel and between the  
17 two planes of trap electrodes 24 & 26 and perpendicular to the  
18 axis of accelerator 7, the analyzer (not shown) and the ion guide  
19 (not shown). The DC electrodes 26 are held at a positive DC  
20 potential during the trapping stage, and the injected electrons  
21 54 are accelerated and decelerated by the DC electrodes 26 as  
22 they enter the trap 20. Magnets 56 and 57 are used to help

1 direct the electrons 54 into trap 20. Slits (not shown) may be  
2 used between the electron filament 58 and trap 20 to remove  
3 divergent portions of the electron beam. Alternatively, the  
4 electron beam could be energy filtered before injection into trap  
5 20. Also, higher energy electrons might be used to ionize  
6 neutral molecules in trap 20. It is possible to produce and  
7 inject the low energy electrons required by ECD into trap 20  
8 because the kinetic energy of the ions in trap 20 is the same as  
9 before they entered trap 20.

10 Turning next to FIG. 8, shown is yet another alternate  
11 embodiment of multiple ion trap 20 according to the present  
12 invention. FIG. 8 depicts low energy electrons 60, from  
13 filament 58, used to produce negative ions from neutral gas phase  
14 molecules. As shown in FIG. 8, the electrons 60 are produced  
15 using filament 58 and introduced from the back of the ion trap 20  
16 since negative ions are to be produced and DC electrodes 26 would  
17 have to be held at negative potentials if the ions were to be  
18 introduced through the top or bottom of trap 20. Electrons 60  
19 will have low kinetic energies and will be able to pass into  
20 multiple ion trap 20 only when the potential on RF/DC electrodes  
21 24 is near zero volts. The RF potential applied to RF/DC  
22 electrodes 24 might be varied from the square wave depicted in

1 diagram 62 of FIG. 8 so that RF/DC electrodes 24 are near ground  
2 potential for a longer period of time. Other waveforms may be  
3 used to enhance the transmission of electrons 60 into trap 20, or  
4 to reduce the electron energy once in trap 20. Once in trap 20,  
5 electrons 60 may ionize molecules according to the "reversal  
6 electron attachment" ("READ") method. To assist in the READ  
7 process, a potential difference may be applied between the two  
8 planes of RF/DC electrodes 24 as well as between adjacent RF/DC  
9 electrodes 24 to "slow down" electrons 60 and then turn them  
10 around while in trap 20. This

11 While the present invention has been described with  
12 reference to one or more preferred embodiments, such embodiments  
13 are merely exemplary and are not intended to be limiting or  
14 represent an exhaustive enumeration of all aspects of the  
15 invention. The scope of the invention, therefore, shall be  
16 defined solely by the following claims. Further, it will be  
17 apparent to those of skill in the art that numerous changes may  
18 be made in such details without departing from the spirit and the  
19 principles of the invention. It should be appreciated that the  
20 present invention is capable of being embodied in other forms  
21 without departing from its essential characteristics.